

Amendments to the Claims

Claim 1 (Currently Amended): An isolated DNA sequence which is selected from the group consisting of (a) encoding for at least part of MonAIV; wherein said at least part of MonAIV is a polypeptide having at least one enzyme activity; and wherein said enzyme activity is selected from the group consisting of ketosynthase activity, acyl transferase activity, dehydratase activity, ketoreductase activity, acyl-carrier protein activity, and enoyl reductase activity ~~the sequence set out in the appended sequence listing; and (b) a variant of a sequence (a) which encodes a polypeptide which is at least 80%, identical with the corresponding peptide as set out in table II; provided that it is not a sequence encoding all or part of the polypeptide consisting of amino acids 1-920 encoded by mon AI as set out in table II.~~

Claim 2 (Currently Amended): A DNA sequence according to claim 1, wherein said DNA sequence comprises ~~comprising~~ the complete monensin gene cluster ~~or a variant thereof.~~

Claim 3 (Currently Amended): A DNA sequence according to claim 1 which encodes for MonAIV which is SEQ ID NO: 22 ~~encoding at least part of at least one polypeptide which is necessary for the biosynthesis of monensin, and which is encoded by DNA included in the appended sequence listing or an allele, mutation or other variant thereof; provided that said polypeptide is not all or part of amino acids 1-920 encoded by mon AI as set out in table II.~~

Claim 4 (Withdrawn): A DNA sequence according to claim 3 which comprises at least part of one or more of the following genes: *mon BI*, *mon BII*, *mon CI*, *mon CII*, *mon H*, *mon RI*, *mon RII*, *mon T*, *mon AIX* and *mon AX*.

Claim 5 (Withdrawn): A DNA sequence according to claim 4 comprising all of the genes listed therein or an allele, mutation or other variant thereof.

Claim 6 (Cancelled)

Claim 7 (Currently Amended): A DNA sequence according to claim ~~[[6]]~~ 1, wherein said polypeptide has ~~6 encoding~~ a single enzyme activity ~~of a multienzyme encoded by any of mon AI mon AVIII or a variant or part thereof.~~

Claim 8 (Currently Amended): A DNA sequence according to claim 1, which further comprises a DNA sequence encoding any one or more of the domains as set out in Table I ~~or a variant or part thereof.~~

Claim 9 (Previously Presented): A DNA sequence according to claim 1 which has a length of at least 30 bases.

Claim 10 (Previously Presented): A recombinant cloning or expression vector comprising a DNA sequence according to claim 1.

Claim 11 (Currently Amended): A transformant host cell which has been transformed to contain a DNA sequence according to claim 1 and which is capable of expressing ~~a corresponding~~ the polypeptide encoded for by said DNA sequence.

Claim 12 (Previously Presented): A hybridisation probe which is a DNA sequence according to claim 1.

Claim 13 (Withdrawn): A method of detecting a PKS cluster comprising using a probe according to claim 12 to detect a PKS cluster, optionally followed by isolation of the detected cluster.

Claim 14 (Withdrawn): A method of detecting genes comprising using a probe according to claim 12 which encodes at least part of a polypeptide having a known function to detect genes encoding polypeptides having analogous function.

Claim 15 (Withdrawn): A method according to claim 14 wherein the polypeptide of known function is AT of module 5 or the regulatory protein encoded by *mon RI*.

Claim 16 (Withdrawn): A hybridization probe comprising a polynucleotide which binds specifically to a region of the monensin gene cluster selected from *mon BI*, *mon BII*, *mon CI*, *mon CII*, *mon H*, *mon RI*, *mon RII*, *mon T*, *mon AIX* and *mon AX*.

Claim 17 (Withdrawn): A method of detecting the presence of a gene cluster which governs the synthesis of a polyether, which comprises using a probe according to claim 16, and optionally isolating a gene cluster detected thereby.

Claim 18 (Withdrawn): A method of detecting a gene comprising using a probe according to claim 12 which comprise a polynucleotide which binds specifically to a gene responsible for levels of activity of the monensin gene cluster, for detecting an analogous gene in a gene cluster for biosynthesis of another polyketide, optionally followed by a step of manipulating the gene detected thereby to alter the level of expression of said other polyketide.

Claim 19 (Withdrawn): A method according to claim 18 wherein the gene is a regulatory gene, resistance gene or thioesterase gene.

Claim 20 (Withdrawn): A method of expressing a heterologous gene in *S. cinnamonesis* comprising inserting said gene so that it is expressed under the control of the *mon RI* gene or

variant and a monensin promoter.

Claim 21 (Withdrawn): A method of expressing a polyketide other than monensin which includes using a portion of the monensin gene cluster encoding a polypeptide having chain terminating activity, comprising at least one of *mon AIX* and *mon AX* or a mutant, allele or other variant thereof encoding a polypeptide having chain terminating activity, to effect chain release of said polyketide other than monensin.

Claim 22 (Withdrawn): A method of synthesizing a polyketide other than monensin which includes using a portion of the monensin gene cluster encoding a polypeptide having carbon-carbon double bond isomerase activity comprising at least one of *mon BI* and *mon BII* or a mutant, allele or other variant thereof having isomerase activity to provide a desired stereochemical outcome in the synthesis of said polyketide other than monensin.

Claim 23 (Withdrawn): A polypeptide encoded by a portion of the monensin gene cluster, comprising at least one portion selected from *mon BI* and *mon BII* or a mutant, allele or other variant thereof, having carbon-carbon double bond isomerase activity, or at least one of *mon AIX* and *mon AX* or a mutant, allele or other variant thereof having chain terminating activity.

Claim 24 (Withdrawn): An epoxidase enzyme encoded by *mon CI* or a derivative or variant thereof having epoxidase activity.

Claim 25 (Withdrawn): A cyclase enzyme encoded by *mon CII* or a derivative or variant thereof having cyclase activity.

Claim 26 (Withdrawn): A method for the biosynthesis of a polyketide other than monensin which comprises using a portion

of the monensin gene cluster encoding a peptide having epoxidase or cyclase activity, to provide a said activity in the biosynthesis of said polyketide other than monensin.

Claim 27 (Withdrawn): A process for producing a polyketide containing a desired starter unit comprising providing a PKS gene having a loading module and a plurality of extension modules, wherein the loading module includes a KS_q domain derived from a KS domain of a monensin extension module.

Claim 28 (Withdrawn): A process according to claim 27 wherein the KS_q domain is derived from KS of module 5 of monensin.

Claim 29 (Withdrawn): A process according to claim 27 wherein the starter unit also includes an AT_q domain derived from an AT domain which is naturally associated with the KS domain.

Claim 30 (Currently Amended): A DNA sequence comprising DNA encoding at least one polyketide synthase (PKS) loading module and a plurality of PKS extension modules, and which can be expressed to produce a polyketide; wherein at least one of said modules or at least one domain thereof is a monensin module or domain ~~or a variant thereof~~ from MonAIV and is contiguous to said PKS loading module or a further one of said modules or a domain PKS extension module or domain to which ~~it~~ said monensin module or domain from MonAIV is not naturally contiguous; provided that the sequence is not an ~~ery~~ erythromycin loading module, the first and second extension modules of the ~~ery~~ erythromycin PKS and the ~~ery~~ erythromycin chain-terminating thioesterase in which the DNA encoding acyltransferase (AT) of the first extension module has been substituted by DNA encoding an ethyl malonyl-CoA AT from the monensin gene cluster.

Claim 31 (Original): A DNA sequence according to claim 30 wherein said further module or domain is also a monensin module or domain or variant thereof.

Claim 32 (Currently Amended): A DNA sequence according to claim 30 wherein said further module or domain is a module or domain of a PKS of a polyketide other than monensin ~~or a variant thereof~~.

Claim 33 (Previously Presented): A DNA sequence according to claim 30 wherein said loading module is adapted to load a starter unit other than a starter unit normally received by the adjacent extension module.

Claim 34 (Currently Amended): A DNA sequence according to claim 33 wherein said loading module ~~is~~ comprises a KSq domain derived from a ketosynthase (KS) domain of a monensin extension module ~~or variant thereof~~.

Claim 35 (Withdrawn): A polyketide synthase encoded by the DNA sequence of claim 30.

Claim 36 (Withdrawn): A polyketide compound as produced by a synthase according to claim 35.

Claim 37 (Previously Presented): A vector containing a DNA sequence of claim 30.

Claim 38 (Previously Presented): A transformant cell transformed to contain a DNA sequence of claim 30.

Claim 39 (Withdrawn): A method of producing *S. cinnamonensis* capable of enhanced levels of production of monensin comprising engineering it to overexpress the *mon RI* gene.

Claim 40 (Withdrawn): A method according to claim 39 wherein

said engineering comprises introducing at least one additional copy of the *mon RI* gene as shown in the appended sequence data or a variant thereof.

Claim 41 (Withdrawn): *S. cinnamomensis* containing multiple copies of the *mon RI* gene as shown in the appended sequence data and/or variant(s) thereof.

Claim 42 (Withdrawn): A method of producing monensin comprising culturing the organism of claim 41.

Claim 43 (Withdrawn): A process for expressing a gene heterologous to *S. cinnamomensis* comprising transforming *S. cinnamomensis* with DNA encoding a heterologous gene and expressing said gene under control of the activator gene *mon RI* or *actII/orf4*.

Claim 44 (Withdrawn): A process according to claim 43 wherein said heterologous gene is a PKS gene.

Claim 45 (Withdrawn) 13-Propyl erythromycin A.

Claim 46 (Currently Amended): A DNA sequence according to claim 1, wherein the amino acid sequence of said polypeptide ~~which is a variant of a sequence (a) which encodes a peptide~~ which is at least 90% identical with the amino acid sequence ~~of the corresponding polypeptide in SEQ ID NO: 22 as set out in table II.~~

Claim 47 (Previously Presented): A DNA sequence according to claim 1 which has a length of at least 60 bases.

Claim 48 (New): A DNA sequence according to claim 1, which is part of nucleotides 12448-24564 of SEQ ID NO: 2.

Claim 49 (New): A DNA sequence according to claim 34, wherein said monensin extension module is from module 5.